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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/527,664	09/19/2005	Christophe de Romeuf	065691-0389	5235

22428 7590 07/22/2008
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EXAMINER	
DAHLE, CHUN WU	

ART UNIT	PAPER NUMBER
1644	

MAIL DATE	DELIVERY MODE
07/22/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/527,664	DE ROMEUF ET AL.	
	Examiner	Art Unit	
	CHUN DAHLE	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 February 2008 and 28 March 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2 and 22-42* is/are pending in the application.

4a) Of the above claim(s) *30 and 34-37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,22-29,31-33 and 38-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *03/11/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment to the claims, filed on February 13, 2006, is acknowledged.

Claims 3-21 have been canceled.
Claims 1, 2, 22-42 are pending.

2. Applicant's election with traverse of anti-HLA-DR antibody capable of inducing TNF, filed on March 28, 2008, is acknowledged.

Upon reconsideration, the prior art search has been extended to cover all cytokines produced by the effector cells.

The traversal is on the ground that the claimed antibodies exhibit corresponding special technical features over the prior art in that the claimed invention is directed to particular antibodies capable of inducing cytokine production in effector cells. Applicant argues the prior art Harris et al. (although describe antibodies made in YB2/0) do not teach antibodies made in YB2/0 would induce cytokine production in effector cells. Applicant asserts that YB2/0 does not always produce antibodies that have the features as claimed. Thus, applicant argues that the restriction requirement should be withdrawn.

This is not found persuasive for reasons of record set forth in previous Office Action mailed on December 12, 2007. In addition, contrary to applicant's assertion that the claimed invention is directed to particular antibodies, it is noted that independent claim 1 is drawn to a generic human or humanized antibody without antigen specificity recited. Further, in contrast to applicant's assertion that YB2/0 cells doe not always produce antibodies that have the claimed features, the instant claims as written, does not set forth any conditions required for YB2/0 to produce antibodies as claimed (e.g. see claim 28). Furthermore, applicant has not provided any objective evidence to show YB2/0 would not produce antibodies as claimed. Therefore, applicant's arguments have not been found persuasive.

Given that species of different antibodies are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1, the species election requirement is deemed proper and therefore made FINAL.

Claims 30 and 34-37 have been withdrawn from further consideration under 37 C.F.R. 1.142(b) as being drawn to nonelected species.

Claims 1, 2, 22-29, 31-33, and 38-42 are currently under consideration as they read on the elected species of an anti-HLA-DR antibody.

3. Applicant's IDS filed on March 12, 2005, is acknowledged. Only US Patent 6,180,377 has been considered. The foreign references and non-patent literature documents listed on IDS are not considered because applicant fails to submit copies of those references.

4. The specification is objected to for following informalities:

The use of trademarks has been noted in this application (e.g. RITUXAN in Table 1 on pages 8-9). Each letter of the trademarks should be capitalized wherever it appears and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks. Appropriate correction is required.

5. Claims 1, 2, 22-29, 31-33, and 38-4 are objected to for following informalities:

A) Claims 1, 2, 22-29, 31-33, and 38-4 are objected to because of the recitation of "humanized chimeric monoclonal antibody". Applicant is required to clarify whether the claimed monoclonal antibody is humanized or chimeric.

B) Claims 31-33 are objected to because they are dependent upon withdraw claim 30. For examination purposes, claim 31 is read as dependent upon claim 1.

C) Claims 2, 32, 35, and 38 are objected to due to the recitation of "CD16 receptor expressing effector cells" because CD16 is a cell surface receptor. Applicant is suggested to amend the claims to "CD16 expressing effector cells".

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1, 2, 22-29, 31-33, and 38-42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 1, 2, 22-29, 31-33, and 38-4 are indefinite in the recitation of "wherein said antibody has an ability ...." (see line 6 of claim 1) because the metes and bounds of the said antibody is unclear and ambiguous. It is not clear whether "said antibody" is referred to the human or humanized chimeric monoclonal antibody or the same antibody produced in a CHO line or commercially available homologous antibody.

B) Claims 27, 28, and 33 are indefinite in the recitation of "in particular" because the metes and bounds of the claims are unclear and ambiguous. Description of examples or preferences is properly set forth in the specification rather than the claims. The examples or preferences, when stated in the claims, would lead to confusion over the intended scope of the claims. It is not clear whether the claimed narrow range encompassed by "in particular" is a limitation.

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claim 32 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This is a *Written Description*, New Matter rejection.

The phrase "the expression line for apolizumab" as recited in claim 32 is not supported by the original disclosure or claim as filed.

Applicant's amendment, filed on February 13, 2006, does not direct to support in the specification for the added new limitation and does not assert that no new matter has been added.

However, the specification as filed does not provide sufficient written description of the above-mentioned "limitation". The specification does not provide sufficient support for "the expression line for apolizumab". The instant claim now recites the limitation which was not clearly disclosed in the specification. Therefore, the claim represents a departure from the specification and claims originally filed.

Such limitations recited in the present claims, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

Applicant is required to cancel the new matter in the response to this Office Action.

Alternatively, applicant is invited to provide sufficient written support for the "limitations" indicated above. See MPEP 714.02, 2163.05-06 and 2173.05 (i).

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 1, 2, 22-29, and 38-42 rejected under 35 U.S.C. 102(b) as being anticipated by Beliard et al. (WO 01/77181) as evidenced by Beliard et al. (US Patent Application US 2003/0175969).

It is noted that Beliard et al. (WO 01/77181) is in French. However, given that Beliard et al. (US Patent Application US 2003/0175969) is the national stage under 35 U.S.C. 371 of PCT international application PCT/FR01/01127 that is published as Beliard et al. (WO 01/77181), Beliard et al. (US Patent Application US 2003/0175969) is deemed to be the English translation of Beliard et al. (WO 01/77181). Thus, the rejection is based on the content of Beliard et al. (US Patent Application US 2003/0175969).

Beliard et al. teach human anti-Rhesus D monoclonal antibody made in rat myeloma host cell YB2/0 that has particular glycosylation profile in the Fc region wherein said human anti-Rhesus D monoclonal antibody exhibits enhanced CD16 mediated ADCC function compared to commercially available homologous antibodies (e.g. see Examples 1-3 on pages 6-17).

Given that the prior art human anti-Rhesus D monoclonal antibody is made in the same YB2/0 host cells as the claimed antibody, the prior art antibody would inherently have the properties, e.g. an ADCC rate of greater than 100% at a concentration of 10/ng/ml or less, induction of cytokines such as interleukine or TNFs by Jurkat CD16 cells or CD16 expressing effector cells of the immune system. Since the office does not have a laboratory to test the reference antibodies, it is applicant's burden to show that the reference antibodies do not have the properties as recited in the claims. See *In re Best*, 195 USPQ 430, 433 (CCPA 1977); *In re Marosi*, 218 USPQ 289, 292-293 (Fed. Cir. 1983); *In re Fitzgerald* et al., 205 USPQ 594 (CCPA 1980).

Therefore, the reference teachings anticipate the claimed invention.

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 1 and 31-33 is rejected under 35 U.S.C. 103(a) as being unpatentable over Tso et al. (US Patent 6,894,149) in view of Ogawa et al. (EP 1229125, published on July 8, 2002).

Tso et al. teach a method for treating diseases such as chronic myeloid leukemia by administering humanized anti-HLA-DR monoclonal antibody (e.g. see columns 4 and 7-8). Tso et al. further provided methods of genetically engineering of the anti-HLA-DR antibodies and working examples of method of making anti-HLD-DR antibodies using conventional hybridoma techniques (e.g. see columns 6 and 14).

The reference teachings differ from the claimed invention by not describing humanized anti-HLA-DR antibody made in rat myeloma YB2/0 cells.

Ogawa et al. teaches that antibodies e.g. humanized antibodies, made in YB2/0 host cells, have a higher antibody-dependent cell-mediated cytotoxic activity (ADCC) and are useful as a pharmaceutical agents for treating diseases such as cancer (see entire document, particularly columns 3-5). Ogawa et al. teach that cDNA encoding antibodies can be cloned from known hybridomas and expressed in YB2/0 cells and the antibodies can be produced in serum free environment (e.g. see column 5).

Given the availability of the hybridomas producing anti-HLA-DR antibodies together with general immunoglobulin gene cloning and expression strategies, it would have been have been a matter of routine experimentation well within the ordinary skill level of art to make humanized anti-HLA-DR antibodies in rat myeloma cell YB2/0. Additionally, such humanized anti-HLA-DR antibodies made in rat myeloma cell YB2/0 would inherently have the properties of an ADCC rate of greater than 100% at a concentration of 10ng/ml or less and a rate of IL-2 production by a CD16 expressing effector cell of the immune system of greater than up to 1000% at a concentration of 10hg/ml or less compared with the same antibody expressed in CHO cell line.

One of ordinary skill in the art would have been motivated to make humanized anti-HLA-DR antibodies taught by Tso et al. in YB2/0 cells for enhanced ADCC function for therapeutic regimens in humans in view of the teachings from Ogawa et al. of the advantage of producing antibodies in YB2/0 cells. One of ordinary skill in the art would have had a reasonable expectation of success in generating humanized anti-HLA-DR antibodies in YB2/0 cells and used said antibodies in a method of treating chronic myelocytic leukemia. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

11. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference

claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

12. Claims 1, 2, 22-29, 31-33, and 38-42 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over:

Claims 64-80, 86, 88, 90-93 of copending Application No. USSN 10/551,819,
Claims 18, 19, and 21 of copending Application No. USSN 10/575,218,
Claims 19-38 of copending Application No. USSN 11/039,877.

Although the conflicting claims are not identical, they are not patentably distinct from each other because both the instant and the copending application claims are drawn to same or nearly the same antibodies that are made in host cells including YB2/0 that would add specific N-glycan to the Fc region of the antibodies. It is further noted that the instant claims 1, 2, 22-29, and 38-42 recite a genus of human or humanized antibody without reciting antigen specificity or antibody class. In turn, the species recited in copending claims (e.g. antibody that binds antigen rhesus D in claim 24 of copending USSN 11/039,877) would thus anticipate the genus of the instant claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

13. No claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chun Dahle whose telephone number is 571-272-8142. The examiner can normally be reached on 8:30-5:00. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Eileen O'Hara can be reached 571-272-0878. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Chun Dahle/
Primary Examiner, Art Unit 1644

Chun Dahle, Ph.D. (formerly Chun Crowder)
Patent Examiner
July 17, 2008